In Vivo Determination of the Complex Elastic Moduli of Cetacean Head Tissue

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LONG-TERM GOALS

The overall goal of this project is to develop and demonstrate a system for non-invasive *in vivo* measurement of the complex elastic moduli (stiffnesses and loss factors) of cetacean head tissues. This system is ultimately intended to provide a portable diagnostic capability for use in stranded animal assessments.

OBJECTIVES

The primary technical objective is to remotely generate and detect mid-frequency elastic waves within the body of a living cetacean and to use the measured propagation parameters of these waves to obtain the complex elastic moduli by inversion. A further technical objective is to extract moduli in this manner for intracranial tissues. This objective carries considerably more technical risk since both the wave-generating ultrasound and the probe ultrasound will be attenuated, distorted and scattered by the passage through the skull. The final objective is to develop a prototype portable version of the technology and use it to perform examinations of stranded animals. Data collected with this system is envisioned to serve two purposes: 1) provide basic knowledge of in-vivo elastic properties, which is non-existent for marine mammals, and 2) provide a potential basis for non-invasive diagnostics of tissue pathologies, both naturally occurring or otherwise induced.

APPROACH

The foundation of the work is the capability to remotely generate elastic waves in soft tissues and observe their propagation with an ultrasound-based non-invasive system. The general approach for generation, reception and interpretation of the tissue wave fields is based on a new medical imaging technology called radiation force elastography[i]. These techniques, which have been demonstrated to some extent on human soft tissues, cannot be directly translated to use on cetacean head tissues due to the need to propagate through much thicker tissues and through skull bone, all the while keeping within safety limitations for ultrasound exposure[ii]. The current focus of the *in-vivo* program is to overcome these challenges through novel redesign of the concepts for both elastic wave generation and observation.

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An embodiment of the shear wave generation system has been developed wherein a ring-like forcing volume is formed by the ultrasonic source. As the ring radius is changed (through a change in the ultrasonic carrier frequency, for example), a fixed receiver measures the change in phase of the waves converging to the center of the ring. This approach has several potential benefits, the sum of which is expected to directly translate to improvements in the robustness of modulus estimation under the challenging constraints of the problem.

The particle displacements resulting from the remotely generated elastic waves are detected remotely using a modified version of an ultrasonic Doppler vibration measurement system called NVMS developed at Georgia Tech[iii]. Algorithms are being developed to enable the magnitude and phase of vibration to be determined, as well as the range (tissue depth) along the ultrasonic beam at which the vibration is being measured. By measuring the arrival time of the shear wave arriving from two different drive distances, as with the ring force excitation, the propagation speed and loss can be determined.

Elastic waves will be both remotely and directly generated in tissue phantoms and measured both remotely and directly to validate the measurement technique. The elastic properties of tissue phantoms will be obtained from remotely generated and measured data and compared with directly measured and tabulated material values. The noninvasive technique will be repeated for tissue phantoms enclosed in a simulated or hydrated real cetacean skull, and with harvested tissue samples. *In vivo* testing will be conducted on Navy dolphins. Ultrasound parameters (peak negative pressure, time averaged intensity) will be consistent with limits established as safe for humans, and ultrasound frequencies will be kept high enough to be far above the highest frequency that is audible to the animals.

WORK COMPLETED

1. System Testing Characterization experiments were conducted using a point-like target, validating basic aspects of ultrasound system operation.

2. Vibrometer Development The depth-discriminating ultrasonic vibrometer used for detecting shear waves in soft tissues was further developed with improvements to signal processing algorithms.

3. Tissue Phantom Development A synthetic material was developed which mimicks the ultrasonic properties of living bottlenose dolphin soft tissues.

RESULTS

1. System Testing The ultrasound system was tested using a point-like target in order to assess remote vibration generation and measurement capabilities. The target, a 0.46 mm diameter stainless steel sphere affixed to a tensioned membrane, was positioned 12 cm from the system transducers, inside a water tank. Motion of the target was generated by the forcing ultrasound transducer (RF), and this motion was separately measured by the vibrometer transducer (NIVMS) and with a laser doppler vibrometer (Polytec PDV-100). A variety of pulse drive levels, durations, and bandwidths for both ultrasound transducers were tested in order to characterize system behavior. An example result is shown in Figure 1, displaying the time domain velocity of the target along the direction of the forcing ultrasound beam. Data from the NIMVS and LDV experiments are shown for a single RF excitation period, with the NIVMS result differentiated with respect to time to compare with the laser, which reports velocity. Also shown in the figure is a prediction of the motion of the target based on pressure

calibrations of the RF transducer, the expected resulting force on the sphere, and a model of the low frequency impedance of the suspended sphere. In the frequency range covered by the data in Figure 1, the dominant impedance is associated with the suspension, and is spring-like, as expected for soft tissues. The measurements are in good agreement with each other, and with the prediction. Of particular significance is the demonstration of ultrasonic motion generation and measurement with the prototype system.

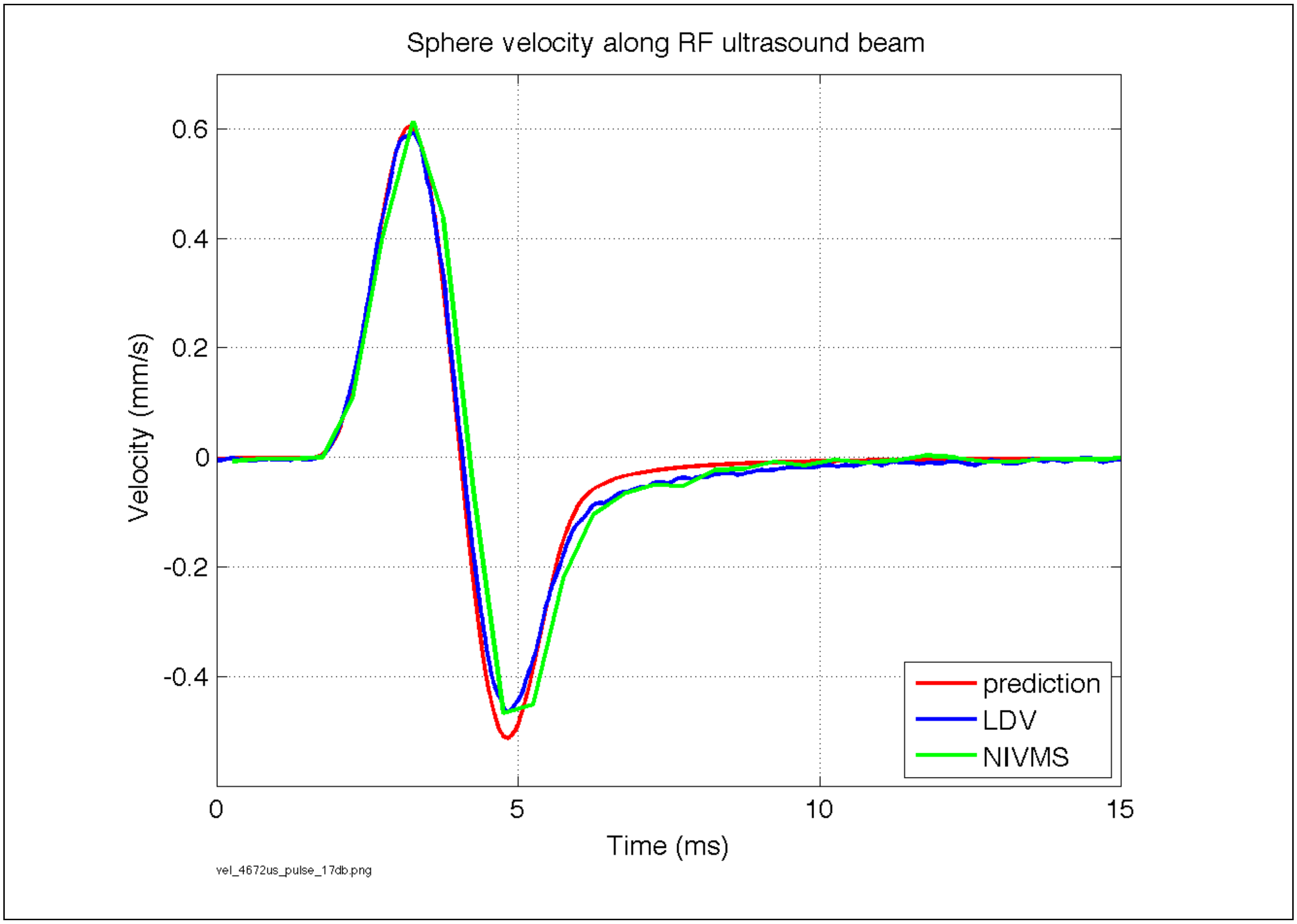

Figure 1. Example of ultrasonically generated sphere target motion during a single forcing pulse period. The predicted time domain motion is shown with laser and ultrasonic vibrometer measurements.

<u>*2. Vibrometer development*</u> Over the past year, work on the range discriminating ultrasonic vibrometer (i.e. NIVMS) focused primarily on pulse compression and the potential to improve the performance of the vibrometer by the selection and proper post processing of an optimal interrogation signal. A post processor was identified that involved a step-wise interpolation of the static transfer function of the system in order to exactly compress the modulated components of the received signal. The limitations of this were analyzed in a series of experiments and numerical simulations. An optimal relationship between the compression pulse and the drive signal amplitude spectra was derived. It can be expressed by the equation:

$$\left|U(\omega)\right|_{optimal} \propto \sqrt{\left|N(\omega)V(\omega)\right|}$$

where U is the optimal interrogation signal, N is the dominant noise in the received signal V is the desired compression pulse, and ω is frequency. The phase of the optimal interrogation signal is determined by minimizing the crest factor of the received signal associated with it. This is therefore tied to the transfer function of the physical system and is not intrinsically unique even when that system is defined. These requirements along with the sampling needs of the vibrometer define all of the salient characteristics of an optimal drive signal. The benefits of optimal signals were evaluated in comparison with likely alternatives. This work is summarized in the manuscript entitled "Pulse compression in a time variant system with application to ultrasonic vibrometry", which was submitted to JASA in July 2012 and is currently being reviewed.

Figure 2 depicts a comparison of the apparent displacement noise that would be measured with various interrogation signals based on a simulation that was seeded with experimental data from an earlier publication. In this case, a simulation was used so that identical noise could be introduced into each realization of the system. The upper plot shows noise as a function of distance from the vibrometer transducer, and the lower plot shows the spectral content of the noise at a single location. The benefit of the optimal interrogation signal and processor in comparison to the direct transmission of the desired pulse can be seen to be about 30 dB for the system parameters that were selected. These are identical to system parameters that have been reported for earlier experimental work: a 2.5 MHz center frequency interrogation signal with 800 kHz bandwidth and 2 kHz periodicity.

3. Tissue Phantom Development A synthetic material for use in system testing was developed in cooperation with a tissue phantom manufacturer. The material was intended to reproduce the ultrasonic attenuation and backscatter strength observed in *in vivo* bottlenose dolphin head soft tissue measurements made in a previous reporting period. Several prototypes were built and tested before arriving at a final formulation. Aside from the ultrasonic properties, the tissue phantom has a relatively low Youngs modulus, although the degree to which it is representative of any living cetacean soft tissues is not yet known. The new tissue phantom material will allow for system testing under more appropriate ultrasonic conditions than previously possible.

IMPACT/APPLICATIONS

There is considerable interest in the development of structural acoustic models for the cetacean head for two main reasons: 1) to better understand biomechanics of sound reception and production in cetaceans, and 2) to understand and hopefully mitigate any harmful effects of man-made sound on their health and behavior. The development and validity of these models is severely limited by an almost complete lack of knowledge of the mechanical properties of the constituent living tissue. There is thus considerable interest in being able to measure these properties *in vivo*. The techniques and instrumentation investigated here should also have biomedical diagnostic application, including non-invasive examinations of stranded animals.

RELATED PROJECTS

None

PUBLICATIONS

1. Martin, J.S., Rogers, P.H. and Gray, M.D., “Pulse compression in time varying systems with applications in ultrasonic vibrometry and tissue elastography”, *163rd meeting of the Acoustical Society of America,* Hong Kong, JASA 131 No.4 Pt. 2 pg. 3290, April 2012.

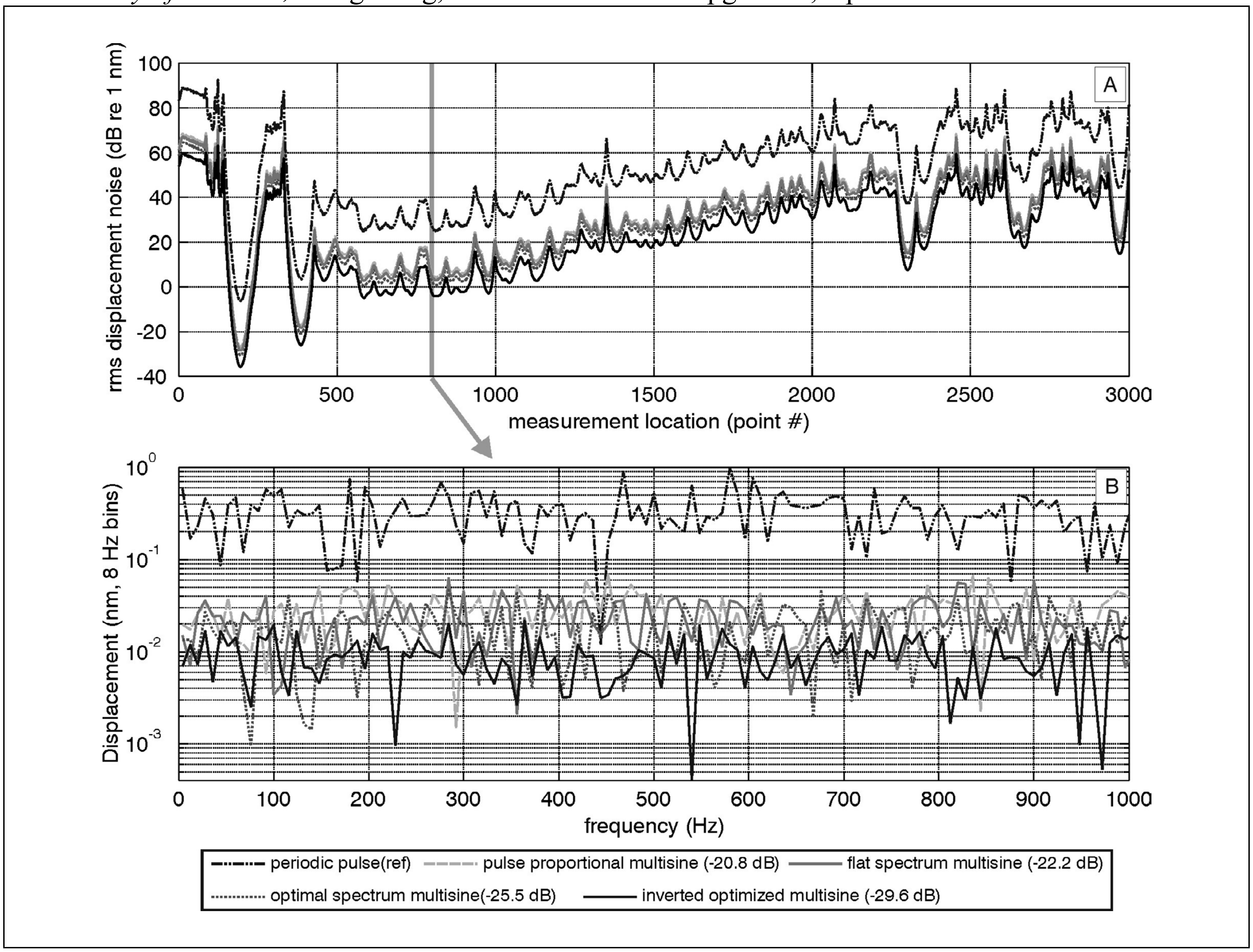

Figure 2. Computed displacement for a simulation with signal-free noise and various interrogation signals. RMS displacement noise as a function of range (A) and spectral content of noise at the 800th range point (B).

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[i] Sarvazyan A, et al, “Shear Wave Elasticity Imaging: a new ultrasonic technology of medical diagnostics”, Ultrasound Med. Biol. 24(9), pp. 1419-1435, 1998

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